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Authors
Choi, Soo Jeong
Obi, Yoshitsugu
Ko, Gang Jee
et al.

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Comparing Patient Survival of Home Hemodialysis and Peritoneal Dialysis Patients

Soo Jeong Choi[a, b] Yoshitsugu Obi[a] Gang Jee Ko[a, c] Amy S. You[a] Rieko Eriguchi[a] Mengjing Wang[a, d] Connie M. Rhee[a] Kamyar Kalantar-Zadeh[a, e, f]

[a]Division of Nephrology and Hypertension and Kidney Transplantation, University of California Irvine School of Medicine, Orange, CA, USA; [b]Division of Nephrology, Department of Internal Medicine, Soonchunhyang University College of Medicine, Bucheon, Republic of Korea; [c]Department of Internal Medicine, Korea University College of Medicine, Seoul, Republic of Korea; [d]Division of Nephrology, Department of Medicine, Huashan Hospital, Fudan University, Shanghai, China; [e]Fielding School of Public Health at University of California-Los Angeles, Los Angeles, CA, USA; [f]Section of Nephrology, Tibor Rubin Veterans Affairs Medical Center, Long Beach, CA, USA

Keywords
Home dialysis · Peritoneal dialysis · Home hemodialysis

Abstract

Background: It is not clear whether peritoneal dialysis (PD) and home hemodialysis (HHD) have similar outcomes, and little is known about how mortality associated with HHD versus PD differs according to the duration of dialysis. ***Methods:*** We examined a national cohort of incident end-stage renal disease patients that was comprised of 1,993 and 16,514 patients transitioning to HHD and PD, respectively, from 2007 to 2011. The HHD patients were matched with PD patients using propensity score (PS). Demographics, comorbidities, duration of dialysis, and body mass index were adjusted for in logistic regression models using PS matching. We matched 1,915 HHD patients with 1,915 PD patients based on the PS. The patients were categorized by their vintage (duration of dialysis) at the time of the transition to HHD or PD (<3, 3 to < 12, and ≥12 months). ***Results:*** In the matched cohort, 237 and 359 deaths occurred in the HHD and PD patients, respectively (cumulative incidence 9.6 vs. 12.9/100 patient-years, $p < 0.001$). PD patients who transitioned within 12 months of starting dialysis had similar mortality risks, while PD patients who transitioned >12 months after starting dialysis had an 83% higher risk for mortality (hazard ratio 1.83; 95% CI 1.33–2.52). ***Conclusions:*** Whereas there was no meaningful survival difference in the first 12 months between HHD and PD, patients who transitioned to PD after 12 months of dialysis had worse survival than their HHD counterparts. Additional studies are warranted to investigate clinical implications of these differences.

Introduction

While most end-stage renal disease (ESRD) patients choose conventional in-center hemodialysis (HD) [1], the use of home dialysis, including home HD (HHD) and

Kamyar Kalantar-Zadeh, MD, MPH, PhD
Harold Simmons Center for Kidney Disease Research and Epidemiology
Division of Nephrology and Hypertension, University of California Irvine
101 The City Drive South, City Tower, Suite 400, Orange, CA 92868 (USA)
E-Mail kkz@uci.edu

peritoneal dialysis (PD), has increased over time [2]. Some experts suggest a "PD first" approach [3]. Many reports have shown that the outcomes of home dialysis are as good as or better than those of in-center HD [4–7]. Recent reports have showed the HHD has a lower mortality risk than home PD [8, 9]. Many reports regarding better survival have focused on frequent or extended HHD [9, 10]. In addition, improved survival has also been found in countries other than the United States [8, 11–14]. Most HHD patients in the United States did not use the frequent or extended form of home dialysis and had a long duration of dialysis [15, 16]. In addition, there are no data regarding whether non-frequent HHD offers better survival than PD. While PD has been established as a first modality, HHD is still undergoing transition as a second modality [15]. In addition, little is known regarding how the mortality rates associated with HHD versus PD differ according to the duration of dialysis at the time of transition. Thus, in the present study, we hypothesized that the timing of the transition to home dialysis (HHD and PD) is associated with survival and that those who transition in the first 12 months of dialysis have the same mortality risk.

Materials and Methods

Patients

We retrospectively extracted, refined, and examined data from all incident ESRD patients who were aged ≥18 years and received dialysis treatment for ≥60 consecutive days in facilities operated by a large dialysis organization in the United States from January 1, 2007, to December 31, 2011 [15]. The data used for the analyses were de-identified. From these patients, we selected those who had started HHD or PD. We then excluded patients who had been treated for <60 days (46,156 patients) and those who had never undergone HHD or PD (141,147 patients). Two thousand eight hundred and forty patients who entered the large dialysis organization >91 days after their 1st dialysis date were excluded (online suppl. Table S1; for all online suppl. material, see www.karger.com/doi/10.1159/000504691). One hundred and seventy patients who underwent both modalities were excluded (online suppl. Fig. S1). This study was approved by the Institutional Review Committee of the Los Angeles Biomedical Research Institute at University of California Irvine Medical Center.

Demographic, Clinical, and Laboratory Measures

Information on death, race/ethnicity, primary insurance, cause of ESRD, comorbidities, and laboratory variables were obtained from the electronic database of the dialysis provider. Data on comorbid conditions were obtained from International Classification of Diseases-9 codes and included diabetes mellitus, hypertension, atherosclerotic heart disease (ASHD), congestive heart failure (CHF), other cardiac diseases (pericarditis and cardiac arrhythmia), cerebrovascular disease, chronic obstructive pulmonary disease, history of cancer, dyslipidemia, liver disease, and alcohol dependence. Blood samples were drawn using uniform techniques in all dialysis clinics and were transported to a central laboratory in Deland, Florida, typically within 24 h. All laboratory values were measured by automated and standardized methods. To minimize measurement variability, all repeated measures for each patient during the first quarter (or 91 days) of HHD or PD were averaged and then used as baseline data in all analyses.

Statistics

For PD, body mass index (BMI) was calculated as the mean of the body weight in kilograms of each patient quarter divided by height in square meters (the absence of a fluid dwell was implied but not explicitly specified) [17]. For HHD, the mean post-dialysis body weight in kilograms for each patient quarter was used for the BMI. Data are presented as the means ± SDs, medians with interquartile ranges, or proportions, as appropriate.

Data were complete for age, sex, diabetes, cause of ESRD, primary health insurance, and cardiovascular morbidities. Data for race was missing for <1% of the cohort. Data for serum creatinine and BMI were missing for 1–4.3% of cohort. Missing covariate data were imputed using a median imputation method in unmatched Cox regressions with an adjustment. The patients were categorized into 3 groups according to the duration of dialysis (<3, 3 to <12, and ≥12 months). The first group was comprised of patients who started maintenance dialysis with HHD or PD as the first modality. The second group was comprised of intermediate transition patients who begin dialysis with other modalities within 3 months and then transitioned to HHD or PD within 12 months. The last group was comprised of the late transition patients, who started with other modalities within 3 months and then changed to HHD or PD after 12 months of dialysis.

For the primary analysis, a propensity score (PS)-matched cohort was constructed to minimize the influence of bias caused by confounders. A logistic regression model was built with HHD as the outcome and the following variables as predictors: age, sex, race, primary health insurance, cause of ESRD, dialysis duration strata (time from first dialysis date to the date of transition to HHD or PD), the presence of comorbid conditions (diabetes mellitus, hypertension, ASHD, other cardiac diseases, CHF, and cerebrovascular disease), and BMI on the transition date. This model was used to calculate the probability of each patient being treated with HHD at the index date (PS). PS were used to identify 1 patient undergoing PD for each HHD patient using greedy matching with a caliper width of 0.2 SDs and without replacement [18]. Standardized differences between the HHD and PD groups in the matched cohort were calculated for each variable and qualitatively compared with the standard differences between the groups in the unmatched cohort to confirm the success of the matching [19].

The patients were followed from their first day of HHD or PD until their death or transfer to HD or kidney transplantation (KTx) or censor date. The primary outcome was all-cause death. For each analysis, the reference group was comprised of patients treated with HHD. Survival was estimated by the Kaplan-Meier method and compared by the log-rank test. For the main intention-to-treat analyses, the index date was the start date of HHD or PD. The participants were followed until the date of death, date of censoring (i.e., transfer to a different dialysis modality, KTx, transfer to a different facility for those undergoing HHD, withdrawal and re-

Table 1. Characteristics of matched incident home dialysis patients (2007–2011) according to time from the first dialysis date to the transition

Variables	Total		SD	<3 months		3–12 months		≥12 months	
	HHD (n = 1,915)	PD (n = 1,915)		HHD (n = 404)	PD (n = 404)	HHD (n = 950)	PD (n = 950)	HHD (n = 561)	PD (n = 561)
Age, years, mean ± SD	54±15	54±15	–0.01	55±15	56±16	54±14	54±16	53±15	52±15
Sex, female, %	35	36	–0.02	34	40	33	30	42	38
Charlson comorbidity index, mean ± SD	5±2	5±2	–0.07	5±2	5±2	5±2	5±2	5±2	4±2
Dialysis duration, median (IQR)	190 (57–421)	158 (55–435)	0.05	19 (9–37)	26 (3–41)	166 (92–254)	134 (81–213)	630 (465–912)	669 (489–935)
Race/ethnicity, %									
Asian	3	3	0.01	4	3	2	3	2	3
African-American	21	23	–0.02	18	23	17	23	30	23
White	68	67	0.02	69	68	74	71	60	58
Hispanic	6	6	–0.02	6	9	5	5	6	7
Other race/ethnicities	2	2	0.02	2	3	2	1	2	2
Primary insurance, %									
Medicare	37	38	–0.02	34	37	36	37	40	39
Medicaid	4	4	0.00	2	2	4	3	6	5
Other	60	59	0.02	64	61	60	60	54	56
ESRD cause, %									
DM	37	38	–0.02	33	37	37	36	41	38
HTN	22	22	0.01	23	21	20	22	24	26
GN	18	17	0.02	16	15	18	18	16	18
PCKD	6	5	0.02	8	8	6	5	4	3
Other	18	18	–0.01	20	19	19	20	15	15
Comorbidities, %									
Diabetes	62	63	–0.02	57	57	61	62	68	68
Hypertension	70	71	–0.02	62	65	70	74	69	75
ASHD	26	26	–0.01	23	19	28	28	29	26
CHF	48	50	–0.04	34	27	47	51	66	61
Cerebrovascular disease	1	2	–0.02	1	2	2	2	1	1
Other cardiovascular disease	22	24	–0.05	21	19	22	25	27	24
COPD	6	8	–0.07	3	6	6	8	8	9
Dyslipidemia	43	51	–0.15	39	50	43	50	52	47
Liver disease	2	3	–0.06	1	3	2	3	2	3
Alcohol abuse	0	0	–0.03	0	0	0	1	0	0
History of cancer	4	3	0.08	3	2	5	2	4	3
Prior transplant	6	4	0.10	5	4	6	4	3	5
BMI, kg/m^2, median (IQR)	28 (24–33)	28 (24–34)	–0.01	28 (24–34)	28 (24–32)	28 (24–34)	27 (24–33)	29 (24–34)	29 (25–34)
Laboratory results, mean ± SD									
Albumin, g/dL	3.9±0.5	3.8±0.4	0.35	3.8±0.5	3.7±0.5	3.9±0.5	3.7±0.4	3.8±0.4	4.0±0.4
Creatinine, mg/dL	7.2±3.0	7.8±3.7	–0.18	5.8±2.1	6.1±2.5	7.0±2.8	7.8±3.6	9.2±4.0	8.6±3.3

HHD, home hemodialysis; PD, peritoneal dialysis; IQR, interquartile range; ESRD, end-stage renal disease; DM, diabetes mellitus; HTN, hypertension; GN, glomerulonephritis; PCKD, polycystic kidney disease; ASHD, atherosclerotic heart disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; BMI, body mass index.

gained renal function) or the end of the follow-up period (December 31, 2011). If a patient died within 60 days after transitioning from a home dialysis modality (HHD or PD) to in-center HD, the death event was attributed to HHD or PD.

To further examine the robustness of our findings, we performed a Cox regression analysis of the entire unmatched cohort (n = 18,507). The models were examined with 3-level hierarchical adjustment levels using the variables listed in Table 1 as follows:

(I) Model 1: unadjusted, and

(II) Model 2: case-mix model adjusted that included demographics (age, sex, race/ethnicity, primary insurance), and case mix covariates (primary ESRD cause; previous transplant; duration of dialysis; and the presence of diabetes, hypertension, ASHD, CHF, other cardiovascular disease, or dyslipidemia),

(III) Model 3: adjusted for Model 2 covariates plus clinical and laboratory variables related to the malnutrition-inflammation-cachexia syndrome, such as BMI and 10 laboratory variables: hemoglobin, serum albumin, creatinine, bicarbonate, uncorrected calcium, phosphorus, intact parathyroid hormone, total iron binding capacity, ferritin, and normalized protein catabolic rate.

Cox proportional hazards assumptions were tested. Analyses were conducted using STATA MP version 13.1 (StataCorp, College Station, TX, USA).

Table 2. Follow-up, number of events, and event rate by modality in the propensity score-matched (n = 3,180) cohorts

Modality	Patient-years of follow-up	Mortality		Transfer to in-center HD		Transplanted	
		events	crude rates (95% CI)*	events	crude rates (95% CI)*	events	crude rates (95% CI)*
Matched							
HHD	2,474	237	9.6 (8.4–10.9)	420	17.0 (15.4–18.7)	216	8.7 (7.6–10.0)
PD	2,787	359	12.9 (11.6–14.3)	478	17.2 (15.7–18.8)	157	5.6 (4.3–6.6)

* Rate per 100 person-years.
HHD, home hemodialysis; PD, peritoneal dialysis.

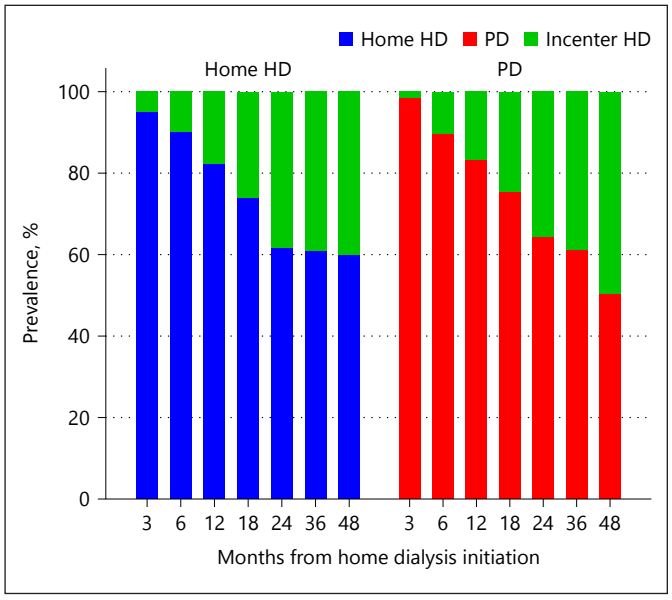

Fig. 1. The distribution of home dialysis modality and treatment time in the 3,830 matched patients. HHD, home hemodialysis; PD, peritoneal dialysis.

Results

Baseline Demographic, Clinical and Laboratory Characteristics of the HHD and PD Study Populations

Between January 1, 2007, and December 31, 2011, 1,993 and 16,514 patients started HHD and PD, respectively (online suppl. Table S2). Compared with the PD patients, the HHD patients were younger; had more comorbidities; were more likely to be male, white and non-Hispanic; were less likely to be enrolled in Medicare; were likely to have hypertension, cardiovascular comorbidities, and previous KTx history; and had higher baseline serum albumin and creatinine levels. The HHD patients had a longer duration of dialysis (median 195 vs. 37 days, $p < 0.001$) and shorter home modality time (264 vs. 367 days, $p < 0.001$) compared with the PD patients.

For each of 1,915 (96.1%) HHD patients, we identified 1 matched PD patient. The mean age of the HHD patients was 54 ± 15 years, and 65 and 68% of the HHD patients were male and white, respectively. There were no meaningful differences between groups in the matching variables (Table 1).

We identified 404, 950, and 561 patients who transitioned to HHD within 3 months, 3–12 months and 12 or more months since after the start of dialysis, respectively.

Overall Outcome Analyses

During the follow-up period, 898 patients in the matched group transferred to in-center HD. A total of 596 patients died, while 373 underwent KTx. The crude rates for mortality, transfer to in-center HD and KTx for the matched groups are shown in Table 2. While more HHD patients underwent transplantation, the same rates of patients transferred to in-center HD in the matched cohort. Figure 1 shows the patient treatment modality distribution during the observation period (interval from the start of HHD/PD to the censor date). More HHD patients than PD patients transferred to in-center HD within 12 months. The PD patients had a greater mortality rate than the HHD patients in the matched group (cumulative incidence 12.9 vs. 9.6/100 patient-years, $p < 0.001$; Table 2).

We sub-analyzed mortality according to duration of dialysis (<3, 3 to <12, and ≥12 months) in Figure 2. The PD patients who transitioned within 12 months from the start of dialysis had no significant difference in mortality risk compared with the patients who transitioned to HHD within 12 months from the start of dialysis (Fig. 2a, b). Only PD patients who transitioned >12 months after the start of dialysis had a higher risk of mortality (hazard ratio 1.83; 95% CI 1.33–2.52; Fig. 2c).

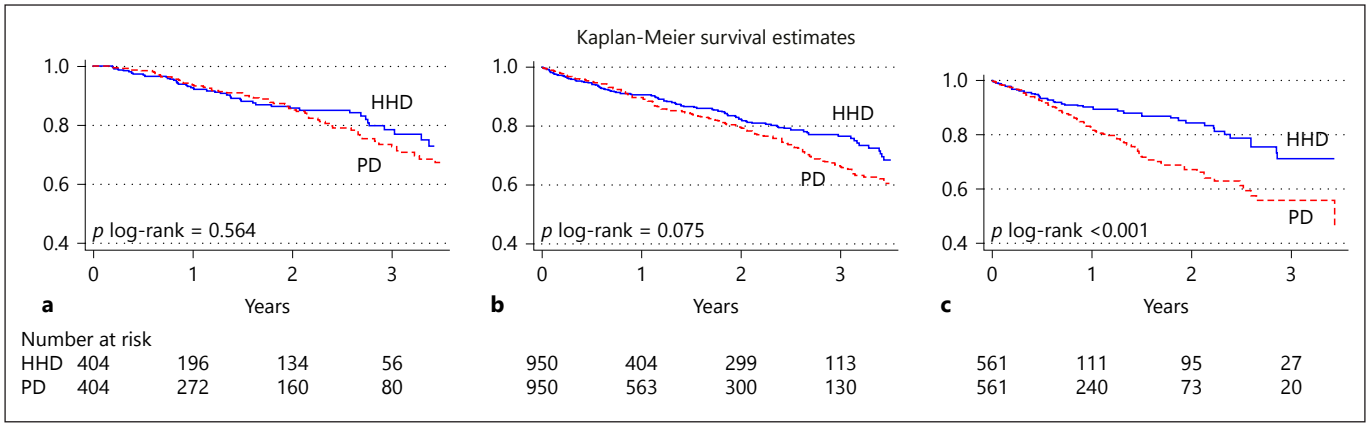

Fig. 2. Kaplan-Meier survival curves of the matched home dialysis cohort according to dialysis duration <3 months (**a**), 3–12 months (**b**), and ≥12 months (**c**) at transition time. HHD, home hemodialysis; PD, peritoneal dialysis.

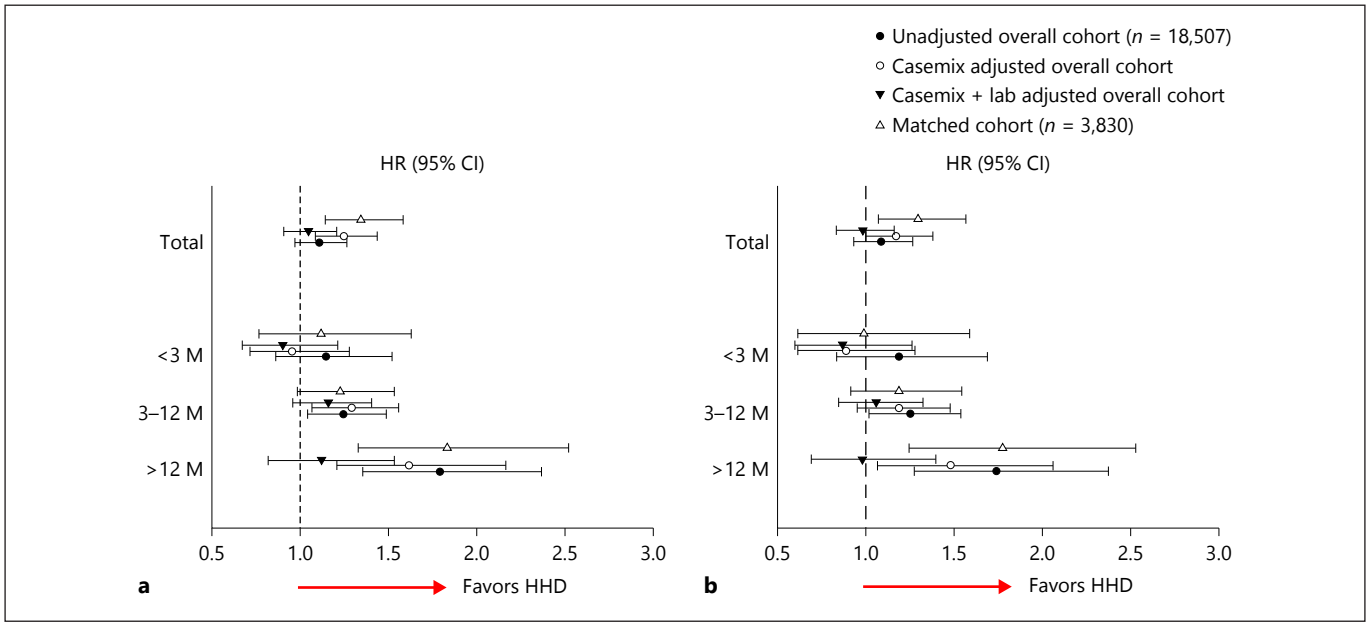

Fig. 3. The impact of dialysis duration at transition time of HHD and PD on all-cause mortality among the unmatched cohort and the matched cohort in the intention-to-treat analysis (**a**) and on-treatment analysis (**b**). HHD, home hemodialysis; HR, hazard ratio; M, months.

Regarding sensitivity, a Cox regression analysis of the entire unmatched cohort showed that duration of dialysis was associated with different risk for all-cause mortality in the intention-to-treat analysis and on-treatment analysis (Fig. 3 and online suppl. Table S3). In the unmatched cohort, patients who started PD as the first modality within 3 months of starting dialysis had mortality risk that were similar to those of the patients who started HHD within 3 months of starting dialysis.

Discussion

In a large national cohort of home dialysis patients in the US, we sought to compare survival amongst HHD and PD patients who were matched on the basis of PS. In this study, we found that these 2 home dialysis modality groups had similar survival in the first 12 months of treatment. However, patients who transitioned to PD after 12 months of dialysis had worse survival than their HHD

counterparts. Given that our study focused on comparisons within the home dialysis population (who may be inherently more similar than those receiving in-center HD), as well as our use of propensity-score matching, we were able to make comparisons across HHD and PD patients whose characteristics were more well-balanced than past comparative effectiveness studies [20–24].

A recent Australian and New Zealand Dialysis and Transplant Registry (ANZDATA) study showed better survival in 706 incident HHD patients compared with 10,710 incident PD patients [8]. While their study included all forms of HD performed in a home setting (conventional, long, frequent, or long/frequent sessions), it excluded patients who received home dialysis within 90 days of starting renal replacement therapy; this led to possible survivor bias given that many patients on HHD receive sustained in-center HD treatment before transitioning to HHD [13]. While recent studies have shown that daily HHD has better outcomes than PD, they suggested examining the effect of duration on outcomes [9–11]. The duration effect might be due to the difference in the amount of time that each modality is prescribed. In our previous study, we reported that HHD treatment occurred an average of 3.7 times per week for 165 min per session, and most patients transferred to HHD after long-term in-center HD (median 610 days) [15, 25]. ANZDATA reported that conventional HHD patients were 2.4 times more common than frequent HHD patients and that both modalities had similar mortality rates [11]. The Canadian Organ Replacement Register study reported 46, 39, and 15% of HHD cases are receiving conventional, nocturnal and short daily HD, respectively [26]. They showed short daily, nocturnal and conventional home HD have similar patient and treatment survival.

To overcome these limitations of prevalence and the non-daily pattern of the American data, we selected a large cohort of patients undergoing HHD or PD. Our cohort excluded 2,840 patients whose modality history was unclear because they had started >91 days after their 1st dialysis date (online suppl. Table S1). The excluded patients had longer dialysis duration (median 405 days) and included more Medicare patients. In the unmatched cohort of 18,507 patients, all 21% of the HHD patients and 53% of the PD patients transitioned within 3 months after 1st dialysis date. Previous reports revealed that the percentage of patients who started HHD within <6 months after the start of dialysis ranged from approximately 10–32% as a result of a "home dialysis first" policy [9, 10, 27]. These rates of early transition were relatively high, while only 12 and 34% of patients had received information about HHD and PD, respectively, when they started dialysis [28]. While PD has been established as the first modality, HHD is still considered a second modality [15]. We included all 1,993 HHD patients of all dialysis durations and compared them with the patients in the study by Nadeau-Fredette et al. [8]. A total of 18% of patients who had ever undergone HHD started with HHD as their first modality. In addition, fewer HHD patients continued with that modality after 12 months compared with PD patients (27 vs. 50%, $p < 0.001$). This discontinuation result was higher than previous reports [10, 29, 30]. Seshasai et al. [29] reported 24.9% of 1 year incidence of discontinuation in 2,840 HHD cohort with long vintage (median 2.1 years) while others reported 18–22% discontinued at 1 year of follow-up. PD is internationally less costly compared with in-center HD [31], and is cost effective even if patients revert to in-center HD due to technical failure within 1 year [32]. Therefore, our results suggest we have to focus on non-inferiority of PD within early transition (within 12 months) rather than HHD superiority beyond 12 months of vintage [10]. Suri et al. [33] reported >80% of the modality failures occurred within the first year, while >90% occurred by 2 years in daily HHD and PD patients. ESRD patients should be informed of all modality options, especially home dialysis [28], and might start PD as a first modality and transition to HHD as a second modality.

We found that HHD and PD patients had the same overall mortality in the unmatched cohort, while PD had a higher overall mortality rate than HHD in the matched cohort (online suppl. Table S3). In addition, the PD patients who transitioned within 1 year had the same mortality risk as the HHD patients. Weinhandl et al. [10] reported that the all-cause mortality and 1-year mortality of patients who initiated daily HHD within 6 months after the start of dialysis were the same as those of patients who initiated PD within 6 months. This duration effect is consistent with previous ANZDATA reports [12]. In addition, the benefit of PD for survival within the first 12–24 months was consistent with previous reports [34–36]. Our HHD patients had a shorter duration of dialysis (190 days) because we included incident ESRD patients who transitioned within 91 days after the first dialysis date, unlike previous reports (online suppl. Table S1). Technical failure of HHD is less common than that of PD [8, 10]. The incidence of technical failure in PD was similar to that of HHD in the matched cohort, which was lower than previous reports [10, 25, 27, 29]. We could not explain the exact cause of the short duration effect. The rates of cardiovascular and infectious causes of death (data not shown) were similar between the matched HHD and PD

patients, which differs from previous reports [10, 33]. Cachexia and withdrawal of PD patients were suggested as causes of increased mortality in a previous report that indicated that HHD patients had a better quality of life [7, 37]. In addition, the fluid overload effect in PD patients might be delayed within the first 12 months [38]. However, these results are very similar to those of many previous PD and in-center HD studies [3, 5, 34, 35, 39].

This study has important strengths. First, we examined longitudinal data from a national large dialysis organization with detailed patient-level data on socio-demographics, comorbidities, and laboratory data. Second, we also used a more rigorous method to account for differences among home HD vs. PD patients than other approaches (i.e., multivariable adjustment), and even after matching had a large, robust cohort of home dialysis patients. Third, we evaluated patients who recently started home dialysis in the United States and compared the outcomes between modalities. Although the ESRD prospective payment system is associated with the increased use of home dialysis, home dialysis is not familiar to nephrologists and patients in the United States, and gaps exist between modalities [2, 28, 42, 43]. Fourth, we focused on the effects of dialysis duration (vintage) on mortality. While ESRD patients may transition across various modalities over time, little is known about how mortality associated with HHD versus PD differs according to the duration of dialysis at the time of transition. We revealed no mortality difference was noted in patients transferring to home dialysis (HHD or PD) with <12 months of in-center HD. If patients plan for home dialysis as RRT, the type of home dialysis should not only be considered, but also the transition time to home dialysis. A timely home to home approach thus stands to capitalize on the benefits of the 2 complementary forms of RRT while minimizing their individual limitations [42].

However, there are important limitations to our study. First, although PS matching may have provided a more rigorous approach for accounting for confounders, we cannot exclude the possibility of residual confounding as well as potential selection bias. For example, we observed higher rates of KTx in the matched home HD vs. PD patient, and it is possible that, despite PS matching, the home HD patients may have been healthier than those receiving PD due to potential self-selection or provider bias. Second, given the retrospective nature of our study, we also concur that we cannot determine whether all patients had equal access to all dialysis modality types, nor indications for which patients transitioned to specific dialysis modalities Third, we did not match upon laboratory data at transition time because there was no information on the laboratory results before transition, and only data on the transition quarter were available. In addition, we did not have time-updated information on comorbidity status over patients' entire longitudinal courses, and were only able to account for comorbidities at the time of study entry. Fourth we excluded patients who had experienced both modalities although few HHD patients transitioned to PD and vice-versa. Fifth, in our matched study population, we there was a high degree of missingness of data on residual urine volume, and hence we were not able to examine this covariate as a potential confounder or relevant clinical outcome. Due to data limitations, we also did not have formally adjudicated information on cause-of death, and were thus unable to explore mechanistic pathways on this basis.

In conclusion, we found that there was no significant survival difference among those who transitioned to home dialysis in the first 12 months after starting dialysis, while patients who transitioned to PD 12 months or longer after starting dialysis had worse survival than those who transitioned to HHD after 12 months.

Acknowledgments

This study is based on data provided by DaVita Clinical Research. The article has been reviewed and approved by DaVita. The interpretation and conclusions are those of the authors and do not represent the views of DaVita.

Portions of these data have been accepted an oral abstract presentation at the American Society of Nephrology Kidney Week Conference, from October 31 to November 5, 2017, New Orleans, LA, USA.

Disclosure Statement

K.K.-Z. has received honoraria from Abbott, AbbVie, Alexion, Amgen, AstraZeneca, AVEO, Chugai, DaVita, Fresenius, Genentech, Haymarket Media, Hospira, Kabi, Keryx, Novartis, Pfizer, Relypsa, Resverlogix, Sandoz, SanofiAventis, Shire, Vifor, UpToDate and ZS Pharma.

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Author Contributions

K.K.-Z., S.J.C. conceived and designed the study. S.J.C., Y.O., A.S.Y., and G.J.K. acquired, analyzed the data, wrote the manuscript. S.J.C., Y.O., and G.J.K. interpreted the data. K.K.-Z., R.E., M.W., and C.M.R. provided advice and revised the manuscript. K.K.-Z. provided supervision or mentorship. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

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